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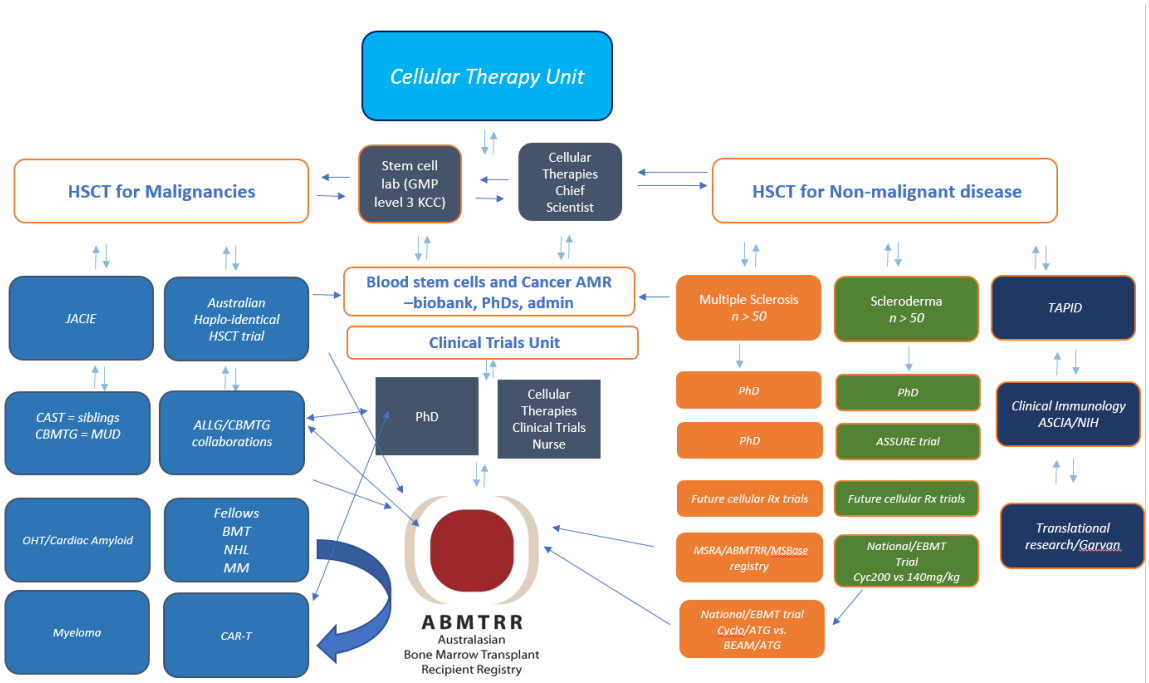
# The ZAMASA Foundation

# STRATEGIC PLAN

# September 2020

**Background : The ZAMASA Foundation**

The ZAMASA Foundation (www.zamasafoundation.org,au) is a research foundation whose mission is to accelerate research into novel therapies in the treatment of multiple myeloma, in particular emerging immunotherapies. The Foundation was formally established as a Registered Charity in NSW in 2017. Working closely with the Haematology and Bone Marrow Transplant Department of St Vincent's Hospital in Sydney and the St Vincent's Curran Foundation, in 2019, the Foundation established the ZAMASA Myeloma Fellowship at St Vincent's Hospital, the first Myeloma Fellowship in New South Wales. St Vincent's was selected as the hospital for the establishment of this fellowship in light of their credentials in the field of haematopoietic stem cell transplantation and genomics. This Fellowship has been incorporated into the strategic plan of St Vincents Hospital to develop a Centre of Excellence in Cellular Therapies at St Vincent's Hospital. This Centre of Excellence is an integral part of the long-term strategy of St Vincents and Mater Health Australia. It will provide a unique opportunity to lead a clinical and research team dedicated to improving outcomes in haematopoietic stem cell transplant for patients with autoimmune and malignant conditions whilst implementing emerging cellular and immune therapies. As outlined below in purple, Myeloma therapeutics will be central to the long-term development of cellular therapies. The ZAMASA Foundation will be an integral partner to that vision.



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**Multiple Myeloma in Australia**

Multiple myeloma (or plasma cell myeloma) is a cancer of plasma cells, a type of cell in the bone marrow that is part of the normal immune system. Normal plasma cells produce antibodies, while plasma cells in myeloma usually produce abnormal antibodies (called paraproteins or free light chains) that can be detected on a blood test. Patients are usually diagnosed when they present to their doctor with complications related to the plasma cells in the bone marrow (or related to the abnormal antibody) such as a bony fractures, anaemia (low red cell count), a high calcium level or kidney failure.

Myeloma accounts for 1.4% of all new cancer diagnoses in Australia and is increasing in incidence. The median age of onset is 70 years of age and the expected survival is approximately 6 years. Treatment of multiple myeloma has changed dramatically over the last 20 years with the emergence of immunomodulatory imide drugs (IMiDs) including thalidomide, lenalidomide and pomalidomide and the proteasome inhibitors (PIs) including bortezomib, carfilzomib and ixazomib. More recently, the use of monoclonal antibodies directed against CD38, a protein on the surface of the plasma cell, such as daratumumab and isatuximab, have also been demonstrated to improve outcomes in patients with multiple myeloma. In fit, younger patients, autologous stem cell transplant (using the patient's own stem cells) remains an important part of therapy, even in the novel agent era.

However, multiple myeloma remains incurable in almost all patients. The only potentially curative approach is an allogeneic stem cell transplant (using another person's stem cells) which is associated with significant morbidity and mortality and is not pursued in most patients. Emerging immunotherapy approaches represent the next frontier of myeloma therapy.

**Emerging Immunotherapy Approaches**

New immunotherapy strategies are being studied in multiple myeloma. These include antibody drug conjugates, bispecific antibodies (or bispecific T cell engaged (BiTE) antibodies), chimeric antigen receptor (CAR) T cells and CAR NK cells. All of these novel approaches are undergoing investigation in clinical studies of patients with multiple myeloma.

Antibody drug conjugates target a specific molecule on the cancer cell surface and once bound they deliver chemotherapy directly into the cancer cell. A drug with this mechanism, brentuximab, is used in the treatment of Hodgkin lymphoma Early studies of belantamab, one of these antibody drug conjugates, demonstrate promising results both as a single agent and in combination with bortezomib and dexamethasone in patients with relapsed/refractory multiple myeloma. A number of clinical trials using belantamab in patients with relapsed/refractory multiple myeloma are opening in New South Wales, including at St Vincent's.

T cells are part of the immune system and bispecific antibodies bind to cancer cells and T cells. This binding leads to T cell activation and facilitates T cell killing of cancer cells. Blinatumumab, is an example of a bispecific antibody that is used in the treatment of acute lymphoblastic leukaemia. Early studies of bispecific antibodies in multiple myeloma have demonstrated promising responses, but require further evaluation.

CAR-T cells are T cells that are collected from the patient or a donor and are genetically modified to express a receptor that targets cancer cells. CAR-T cells are currently used in the treatment of acute lymphoblastic leukaemia and B cell lymphomas. CAR-T cells targeting BCMA (B cell maturation antigen) in patients with relapsed and refractory multiple myeloma have demonstrated impressive overall response rates, up to 92% in the Phase I EVOLVE study[1] and 73% in the Karma study[2], however there remain concerns regarding durability of these responses and toxicity of CAR-T cells. In addition, the manufacturing process adds a layer of complexity (and delay in treatment) compared to antibody drug conjugates and bispecific antibodies that are available 'off the shelf'. CAR-NK cells use a different cell of the immune system, Natural Killer cells. The CAR-NK cells are in early studies in multiple myeloma, may be cheaper, associated with less toxicity and available 'off the shelf', and are an exciting prospect in the treatment of patients with multiple myeloma.


1. Mailankody S, Jakubowiak AJ, Htut M, Costa LJ, Lee K, Ganguly S, et al. Orvacabtagene autoleucel (orva-cel), a B-cell maturation antigen (BCMA)-directed CAR T cell therapy for patients (pts) with relapsed/refractory multiple myeloma (RRMM): update of the phase 1/2 EVOLVE study (NCT03430011). Journal of Clinical Oncology. 2020;38(15_suppl):8504-.
   Details: 62 patients in the United States.
2. Munshi NC, Larry D. Anderson J, Shah N, Jagannath S, Berdeja JG, Lonial S, et al. Idecabtagene vicleucel (ide-cel; bb2121), a BCMA-targeted CAR T-cell therapy, in patients with relapsed and refractory multiple myeloma (RRMM): Initial KarMMa results. Journal of Clinical Oncology. 2020;38(15_suppl):8503-.
   Details: 140 patients, sites in Canada, US, Spain, France, Belgium, Germany and Italy.

**The ZAMASA Foundation Strategic Plan**

The ZAMASA Foundation plans to increase patient access to new treatments for Myeloma by a multi-faceted approach as outlined below:

## 1. ZAMASA Foundation Myeloma Fellowship

The ZAMASA Foundation aims to increase patient access to these novel immunotherapy agents in clinical trials within New South Wales. The strategy for this includes ongoing funding of a Myeloma Fellowship at St Vincent's Hospital. Since the commencement of the Myeloma Fellowship, a specific Myeloma Clinic has been established at the Kinghorn Cancer Centre. This allows rapid assessment of patients referred from general practitioners and other hospitals in Sydney and assessment for enrolment in available clinical trials.

With the establishment of the Myeloma Fellowship, St Vincent's has consulted with pharmaceutical companies, The Australasian Leukaemia and Lymphoma Group (ALLG) and the Australasian Myeloma Research Consortium (AMARC) regarding broadening the Myeloma clinical trial portfolio available through the Kinghorn Cancer Centre. Increased availability and access to clinical trials will provide access to novel therapeutic agents and strategies to patients with newly diagnosed and relapsed/refractory multiple myeloma.

The establishment of the Myeloma Fellowship has also led to a number of research opportunities including facilitating collaboration between the Garvan Institute of Medical Research and St Vincent's Hospital in Sydney. A collaborative project with Professor Peter Croucher and A/Professor Tri Phan examining and characterising minimal residual disease following treatment, myeloma cell dormancy and the role of the bone marrow microenvironment in relapse has been commenced across the two sites. This project has been successful in receiving a grant from the University of New South Wales Futures Institute. The access to the Australian Bone Marrow Transplant Recipient Registry (ABMTRR), which is based at St Vincent's Hospital, provides a unique opportunity to evaluate current clinical practice in use of transplantation and cellular therapies in multiple myeloma. The ABMTRR plans to collect data on CAR-T cell recipients and outcomes, and as access to CAR-T cell therapies for multiple myeloma increases in Australia, the unique relationship between St Vincent's and the ABMTRR can be harnessed.

The ZAMASA Foundation Myeloma Fellow has also embarked on other projects. Bortezomib, lenalidomide and dexamethasone induction therapy has just been listed on the pharmaceutical benefits scheme for treatment of newly diagnosed patients with multiple myeloma. The ZAMASA Foundation Fellow is co-coordinating a NSW Harmonisation project to both streamline the use of this new regimen in NSW and examined prescribing patterns, toxicity and outcomes. In addition, they are leading a

project utilising data in the Myeloma and Related Diseases Registry to examining of timing of treatment of first relapse of multiple myeloma and clinical outcomes.

## 2. Myeloma Advanced Practice Nursing

Specialised nursing care has been demonstrated to improve quality of life and continuity of care in cancer patients. Despite the fact that myeloma patients have complex treatment regimens, are often older and have co-morbidities, there are very few myeloma specific nurses and this is an unmet area of need. Availability of myeloma Advanced Practice Nurses would not only have significant benefits to the quality of care provided to individual patients, but would also allow sites to build capacity and increase credibility in participating in clinical trials. With strong support from the ZAMASA Foundation's Medical Advisory Panel, the ZAMASA Foundation is contributing funding for the production of a white paper to collate and present the evidence to support the integration of multiple myeloma Advanced Practice Nurses into specialist myeloma services in NSW. ZAMASA will be contributing funding alongside major pharmaceutical companies, Celgene, Amgen and Jansen.

## 3. Increased Clinical Trial Portfolio and Pharmaceutical Company Engagement

The appointment of the Myeloma Fellow and the establishment of a dedicated Myeloma clinic allows rapid assessment for eligible patients for clinical trials (in particular for cross-referrals). The appointment of a dedicated Myeloma Advanced Practice Nurse would further increase credibility in participating in clinical trials.

We are in the process of setting up two Australian Leukaemia and Lymphoma Group (ALL-G) studies at St Vincent's, FRAIL-M and IRIL. IRIL involves addition of a monoclonal antibody, isatuximab, who achieve an inadequate response to standard therapy. We are hoping to pursue tele-trial opportunities with these ALL-G studies at the regional sites affiliated with St Vincent's (Griffith and Wagga) to increase the access to trials for patients with myeloma in regional areas. In addition, we have been selected as a site for the GlaxoSmithKline trial DREAMM-8 evaluating the addition of belantamab (an antibody drug conjugate) to pomalidomide and dexamethasone.

In addition, in the last 6 months, St Vincent's have established a Master Institutional Confidential Disclosure Agreement with the Celgene Pharmaceutical company. This should allow us increased access to Celgene-led clinical trials including novel agents. We plan to meet with further pharmaceutical companies to establish similar agreements

The goal of the Kinghorn Cancer Centre and St Vincent's Hospital is to increase our multiple myeloma clinical trial portfolio. We aim to provide access to novel therapies, specifically immunotherapies and cellular therapies, for patients in New South Wales with multiple myeloma. By building credibility

with pharmaceutical companies and the ALLG, we seek to become a key site in Sydney for the delivery of these therapies.

## 4. PhD Funding

In the medium term the ZAMASA Foundation aims to contribute funding to motivated PhD candidates who plan to pursue research in Multiple Myeloma and further support the ongoing development of the Cellular Therapies Unit. Priority candidates will have an interest in immune therapy and its application to Multiple Myeloma. The Foundation's Medical Advisory Panel will draft the detailed PHD description. In supporting these early career researchers, the ZAMASA Foundation will expand the volume of Myeloma research within New South Wales, and it is hoped this will provide longer term benefits in terms of better understanding of multiple myeloma and novel treatment approaches.

**Proposed Time Line**

| **2021** | **2022** | **2023** |
|---|---|---|
| ***Specialised Clinical Service at St Vincent's*** | | |
| ZAMASA Foundation Myeloma Fellow as part of Cellular Therapy Unit<br>St Vincent's Myeloma Clinic (cost: $155K pa) | | |
| ***Investigator Initiated Research Projects and Collaborations*** | | |
| Collaboration with Garvan: PreEEMPT Study. Aim Publication 2023. | | |
| Registry Projects Evaluating Current Practice in Multiple Myeloma<br>• Australian Bone Marrow Transplant Recipient Registry<br>• Myeloma and Related Diseases Registry | | |
| NSW VRd Harmonisation Project | | |
| ***Increased Clinical Trial Portfolio*** | | |
| ALL-G FRAIL-M and IRIL<br>Pursue teletrials<br>DREAMM-8 (belantamab) | Bispecific antibodies<br>CAR-T<br>Romosuzumab | |
| ***Myeloma Specialist Nurse*** | | |
| Engagement with NSW Myeloma Working Group White Paper[3] | Employ dedicated Myeloma Clinical Nurse Specialist at St Vincent's (est. $100k/pa) | |
| ***Increase Local Myeloma Research Through PhD Scholarships*** | | |
| | Advertise for PhD Scholarships for Myeloma Research in NSW | PhD Funding (est. a c.$60k/pa) |

[3] At this juncture the ZAMASA Foundation's funding commitment is in relation to funding the ZAMASA Myeloma Fellow at St Vincent's ($155k/pa) and supporting the White Paper ($10k). Future employment of a dedicated Myeloma Clinical Nurse and/or PHD candidate(s) has not yet been contemplated and will be discussed in 2022 with the ZAMASA Medical Advisory Committee and the ZAMASA Foundation Board. A separate funding plan is to be agreed by the Board to ensure the ZAMASA Foundation is well placed to honour any short or medium term strategic commitments.


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